REMARKS

Introductory Comments:

Claims 1-27 were examined in the Office Action under reply and stand variously rejected under (1) 35 U.S.C. §112, first paragraph (claim 27); (2) 35 U.S.C. §102 (claims 1-5, 6, 8, 10, 12 and 14-25); and (3) 35 U.S.C. §103(a) (claims 7, 9, 11, 13 and 18-26). These rejections are respectfully traversed as discussed more fully below.

Applicants acknowledge with appreciation the withdrawal of the previous rejections under 35 U.S.C. §112, second paragraph, as well as the previous art rejections over U.S. Patent No. 6,306,405 to O'Hagan, and over Wyatt et al. (1998) *J. Virol.* 72:1725-1730.

Overview of the Above Amendments:

Claims 1, 4, 5, 6 and 7 have been amended to recite the subject invention with greater particularity. Claim 1 now recites that "the E2 antigen does not include the p7 polypeptide" and that the E2 and E1E2 antigens are "produced intracellularly." Claim 1 has also been amended to recite that a "composition" is administered. Claims 4 and 5 have been amended to replace the term "polypeptide" with the term "antigen" and to recite the term "composition" for antecedent basis purposes. Finally, claim 7 has been amended to delete the clause which includes the amino acid sequence of the E2 plus p7 polypeptide.

Support for these amendments can be found throughout the specification at, e.g., page 3, lines 4-6; page 16, lines 20-24; and page 32, lines 21-22. The foregoing amendments are made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing the unamended claims.

Rejection Under 35 U.S.C. §112, First Paragraph:

Claim 27 was rejected under 35 U.S.C. §112, first paragraph for failure to comply with the written description requirement. Claim 27 depends from claim 1 and recites that the method further comprises administering a polypeptide encoded by the polynucleotide. The Office asserts:

> The specification does not convey that the use of a polypeptide boost was done...The specification does not provide any examples that show that 'boosting with the polypeptide encoded by the polynucleotide used to inoculate the subject is better or produces unexpected results or is different than boosting with the polynucleotide, which is known in the art, see Forns below.
>
> While an original claim may provide support, there is no written description in the specification that indicates that this was the way in which the method was reduced to practice.

Office Action, pages 2-3. However, applicants submit that the Examiner is applying an improper standard for compliance with the written description requirement of 35 U.S.C. §112, first paragraph.

In particular, applicants are not required to reduce an invention to practice in order to comply with the written description requirement of 35 U.S.C. §112, first paragraph. See, e.g., Comment 8 of the PTO Final Examiner Guidelines on Written Description Requirement. Moreover, there is absolutely no requirement that applicants provide unexpected or better results over known methods, as alleged by the Examiner. Rather, in order to comply with the written description requirement, the specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. An applicant may show possession of the claimed invention by describing the claimed invention using descriptive means such as words, structures, figures and the like. See, e.g., Section I of the PTO Final Examiner Guidelines on Written Description Requirement. Based on these tenets, applicants submit that they have indeed complied with the written description requirement of 35 U.S.C. §112, first paragraph.

In particular, the specification explains on page 33, lines 21-22 that "in some embodiments, an immune response is elicited using a prime-boost strategy (one or more DNA-prime and one or more protein-boosts)." Thus, applicants have explicitly stated in words that they were in possession of the subject matter of claim 27. Additionally, subsequent publications have shown that using a DNA prime/protein boost strategy with both E2 and E1E2 may indeed produce an enhanced immune response. See, e.g., Seong et al., *Vaccine* (2001) 19:2955-2964, the abstract of which accompanies this response and

Song et al., *J. Virol.* (2000) 74:2920-2925, also accompanying this response. Thus, the Examiner's concern regarding the efficacy of the prime/boost strategy has been alleviated. Withdrawal of this basis for rejection is respectfully requested.

Rejections Over the Art:

Claims 1-5, 10, 14, 15 and 17-25 were rejected under 35 U.S.C. §102(b) as anticipated by Ishi et al., *Hepatology* (1998) 28:1117-1120 ("Ishi"). The Office argues Ishi discloses eliciting an immune response against an HCV E2 antigen using a polynucleotide encoding E1E2 or full-length E2 that is on the cell surface and is not secreted. However, applicants submit that the claims are not anticipated by Ishi.

The law is clear that in order to anticipate a claim, a single source must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements "arranged as in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983). Finally, the law requires identity between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clar Corp.* 713 F.2d 760, 771, 218 USPQ 2d 781, 789 (Fed. Cir. 1983, cert. denied, 465 U.S. 1026 (1984)).

Ishi does not describe administering an HCV composition. Rather Ishi studied antibody responses to HCV structural proteins in patients infected with HCV virus. HCV virus was not "administered" to patients, as required by the claims. Although the previous claims easily distinguished over Ishi, applicants have clarified that a composition comprising a polynucleotide encoding an HCV antigen is administered. Ishi certainly does not describe administering such a composition. Accordingly, Ishi cannot anticipate the present claims and this basis for rejection should be withdrawn.

Claims 1, 3, 5, 6, 8, 10, 12 and 14-17 were rejected under 35 U.S.C. §102(a) over Forns et al., *Vaccine* (1999) 17:1992-2002 ("Forns"). The Office argues "Forns discloses a polynucleotide that encodes a E2 protein with and without P7 that can be used for eliciting an

immune response to HCV E2." Office Action, page 4. However, as with Ishi above, Forns fails to disclose each and every element of the claimed invention.

In particular, Forns immunized mice with one of three different plasmids as follows: (1) a plasmid containing the entire sequence of the E2 and p7 genes (pE2); (2) a plasmid encoding a truncated form of the E2 protein targeted to the cell surface (pE2surf); and (3) a control plasmid lacking an HCV insert (pDisplay). Forns did not deliver a polynucleotide encoding the full-length E2 gene without the p7 gene, as claimed herein. Nor did Forns administer a polynucleotide encoding an E1E2 antigen, also as claimed. Thus, Forns also does not anticipate the claims and this basis for rejection should be withdrawn.

Claims 7, 9, 11, 13 and 18-26 were rejected under 35 U.S.C. §103(a) as unpatentable over Forns. The Office asserts:

> Knowing the construct of Forns contains all of E2, one of skill in the art would know that it contains the epitopes that give rise to NOB antibodies and it would have been within the skill of one of ordinary skill in the art to assay the antibodies of Forns for NOB antibodies such as with the method as disclosed in Ishi.

Office Action, pages 4-5, bridging paragraph. However, applicants submit that the Office has failed to establish a *prima facie* case of obviousness of the claimed invention over the cited art.

As an initial matter, applicants note that claim 1 was not subject to this rejection. All of claims 7, 9, 11, 13 and 18-26 depend either directly or ultimately from claim 1. Thus, the rejection of claims 7, 9, 11, 13 and 18-26 under 35 U.S.C. §103(a) is improper and for this reason alone should be withdrawn.

Even if the rejection was proper, applicants submit that Forns does not render the claims obvious. It is well settled that *prima facie* obviousness can only be established if the following three basic criteria are met: (1) there must be some suggestion or motivation to modify the reference; (2) there must be a reasonable expectation of success (for the modification and/or combination); and (3) the prior art reference(s) must teach or suggest all the claim limitations. MPEP §2143. Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Applicant's disclosure. *In re Vaeck,* 20 USPQ2d 1438 (Fed. Cir. 1991). The Office has not satisfied these criteria.

In particular, as explained above, Forns did not administer a polynucleotide encoding a full-length E2 protein that lacked the p7 gene, or a polynucleotide encoding an E1E2 protein. Forns does not suggest administering these polynucleotides. Moreover, Forns does not teach or suggest administering a polynucleotide that is produced intracellularly and not secreted when expressed in cells of the subject, as claimed. In fact, Forns specifically targeted the HCV E2 protein to the cell surface. If anything, Forns teaches away from the claimed invention by his observation that cell-surface expressed E2 elicited higher titers of anti-E2 compared to the intracellular form of E2. See, page 1998, second column and page 2000, first column. Accordingly, there is absolutely no expectation of success for applicants' claimed method and no suggestion to modify Forns to arrive at applicants' claimed invention.

Without a suggestion to modify Forns evident in this reference, the only conclusion supported by the record is that the rejection was made impermissibly using hindsight reconstruction of the invention. As stated by the Court of Appeals for the Federal Circuit, "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992). See, also, *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988): "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

Applicants submit, therefore, that the rejection under 35 U.S.C. §103 should also be withdrawn.

CONCLUSION

Applicants respectfully submit that the claims define a patentable invention. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further written communications in this application to:

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